Bosma arhinia microphthalmia syndrome

Bosma arhinia microphthalmia syndrome (BAMS) is a rare condition characterized by abnormalities of the nose and eyes and problems with puberty.

The key feature of BAMS is arhinia, which is the absence of an external nose. While most people with BAMS are born without a nose, some affected individuals have a severely underdeveloped (hypoplastic) nose. Affected individuals may also be missing the brain structure involved in the sense of smell (olfactory bulb). Because of these abnormalities, people with BAMS have an impaired ability to smell and, consequently, to taste.

In most people with BAMS, the eyeballs are abnormally small (microphthalmia) or absent (anophthalmia), which causes severe vision impairment or blindness. Additional eye abnormalities common in BAMS include a gap or hole in one of several structures of the eye (coloboma) and clouding of the lenses of the eyes (cataracts).

Additional head and face abnormalities that can occur in people with BAMS include a high arch or opening in the roof of the mouth (high-arched or cleft palate), absence of the sinuses behind the nose (paranasal sinuses), blockage of the nasal passages (choanal atresia), narrowing of the tear ducts (nasolacrimal duct stenosis), or a small upper jaw (hypoplastic maxilla). Many of these abnormalities contribute to difficulty breathing, particularly in affected babies. Some affected individuals have abnormal external ears.

Individuals with BAMS also have hypogonadotropic hypogonadism, which is a condition caused by reduced production of hormones that direct sexual development. Without treatment, these hormone problems often result in delayed puberty. Affected males may also have underdeveloped reproductive tissues and undescended testes (cryptorchidism).

Frequency

BAMS is a very rare condition with an unknown prevalence. Fewer than 100 cases of the condition have been described in the medical literature. BAMS has been found in several different populations.

Causes

BAMS is usually caused by mutations in the *SMCHD1* gene. Other, unknown genes may be rare causes of the condition.

The *SMCHD1* gene provides instructions for making a protein involved in regulating gene activity by altering the structure of DNA. Specifically, the SMCHD1 protein plays a role in turning off (silencing) certain genes. Among other functions, the SMCHD1

protein appears to be important for development of the nose, eyes, and other structures of the head and face.

Researchers are unsure how *SMCHD1* gene mutations affect the protein's function and lead to the development problems characteristic of BAMS. Changes in this gene may lead to abnormal silencing of genes involved in development of the head and face, which could underlie arhinia, microphthalmia, and other characteristic facial abnormalities of BAMS. Problems with nasal development may affect gonadotropin-releasing hormone (GnRH) neurons, which are nerve cells that control the release of reproductive hormones. GnRH neurons originate in the developing nose and then move to the brain. Impaired development of these neurons could explain hypogonadotropic hypogonadism in affected individuals.

Some people with an *SMCHD1* gene mutation have arhinia without other features of BAMS (isolated arhinia) or less severe abnormalities of the nose, leading researchers to suspect that additional genetic factors contribute to the severity of the symptoms. These additional factors are not yet known.

Inheritance Pattern

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered *SMCHD1* gene in each cell is sufficient to cause the disorder.

Most cases result from new mutations in the gene and occur in people with no history of the disorder in their family. In some cases, an affected person inherits the mutation from one affected parent. The parent often has milder symptoms, such as a reduced sense of smell (anosmia), arhinia without other features of BAMS, or less severe abnormalities of the nose.

Other Names for This Condition

- arhinia choanal atresia microphthalmia
- arhinia, choanal atresia, and microphthalmia
- arhinia, choanal atresia, microphthalmia, and hypogonadotropic hypogonadism
- BAM syndrome
- BAMS
- Bosma syndrome
- Gifford-Bosma syndrome
- hyposmia-nasal and ocular hypoplasia-hypogonadotropic hypogonadism syndrome
- Ruprecht Majewski syndrome

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Arhinia choanal atresia microphthalmia
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1863878/

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22Bosma+arhinia+microphthalmia+syndrome%22+OR+%22arhinia%22

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Hypogonadotropic Hypogonadism
  https://medlineplus.gov/ency/article/000390.htm
- Encyclopedia: Smell - Impaired
  https://medlineplus.gov/ency/article/003052.htm
- Health Topic: Craniofacial Abnormalities
  https://medlineplus.gov/craniofacialabnormalities.html
- Health Topic: Eye Diseases
  https://medlineplus.gov/eyediseases.html
- Health Topic: Taste and Smell Disorders
  https://medlineplus.gov/tasteandsmelldisorders.html

Genetic and Rare Diseases Information Center

- Arhinia choanal atresia microphthalmia
  https://rarediseases.info.nih.gov/diseases/8755/arhinia-choanal-atresia-microphthalmia

Additional NIH Resources

- National Institute of Environmental Health Sciences, Pediatric Neuroendocrinology Group
  https://www.niehs.nih.gov/research/atniehs/labs/crb/pi/pn/index.cfm

Educational Resources

- MalaCards: bosma arhinia microphthalmia syndrome
  https://www.malacards.org/card/bosma_arhinia_microphthalmia_syndrome
- Merck Manual Consumer Version: Overview of Smell and Taste Disorders
  https://www.merckmanuals.com/home/ear,-nose,-and-throat-disorders/symptoms-of-nose-and-throat-disorders/overview-of-smell-and-taste-disorders
- Orphanet: Arrhinia-choanal atresia-microphthalmia syndrome
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=1135
- Orphanet: Hyposmia-nasal and ocular hypoplasia-hypogonadotropic hypogonadism syndrome
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=2250

Patient Support and Advocacy Resources

- Children's Craniofacial Association
  https://ccakids.org/
- Faces: The National Craniofacial Association
  https://www.faces-cranio.org/
- Hormone Health Network
  https://www.hormone.org/
- Microphthalmia, Anophthalmia and Coloboma Support (UK)
  https://macs.org.uk/
- National Organization for Rare Disorders
  https://rarediseases.org/rare-diseases/bosma-arhinia-microphthalmia-syndrome/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28Bosma+arhinia+microphthalmia+syndrome%5BTIAB%5D%29+OR+%28Bosma+arrhinia+microphthalmia+syndrome%5BTIAB%5D%29+OR+%28arhinia,+choanal+atresia,+and+microphthalmia%5BTIAB%5D%29%29+OR+%28%28SMCHD1%5BTIAB%5D%29+AND+%28arhinia%5BTIAB%5D%29%29+AND+english%5Bla%5D

Catalog of Genes and Diseases from OMIM

- BOSMA ARHINIA MICROPHTHALMIA SYNDROME
  http://omim.org/entry/603457

Medical Genetics Database from MedGen

- Arhinia choanal atresia microphthalmia
  https://www.ncbi.nlm.nih.gov/medgen/355084
- Hyposmia-nasal and ocular hypoplasia-hypogonadotropic hypogonadism syndrome
  https://www.ncbi.nlm.nih.gov/medgen/831140

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